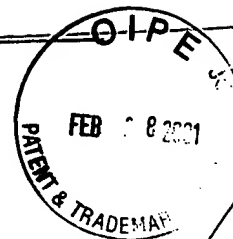




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<110> Sedivy, John
Kolch, Walter
Yeung, Kam Chi

<120> Kinase Inhibitors and Methods of Use in Screening Assays and Modulation of Cell Proliferation and Growth

<130> 3564/1010

<140> 09/654,281

<141> 2000-09-01

<150> 60/151,992

<151> 1999-09-01

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<220>

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<220>

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<222> (14)..(14)

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<220>

<221> UNSURE

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<222> (38)..(38)
<223> Z = a hydrophobic amino acid residue

<220>
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 <222> (39)..(41)
 <223> X = any amino acid residue

<400> 1

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Thr | Leu | Xaa | Xaa | Xaa | Asp | Pro | Asp | Glx | Pro | Xaa | Xaa | Xaa | Asx | Xaa | Xaa |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Xaa | Xaa | Glu | Xaa | Xaa | His | Xaa | Tyr | Xaa | Xaa | Xaa | Xaa | Pro | Xaa | Gly | Xaa |
| | | 20 | | | | | | 25 | | | | | 30 | | |
| His | Arg | Xaa | Val | Xaa | Glx | Xaa | Xaa | Xaa | Gln | | | | | | |
| | | 35 | | | | | | 40 | | | | | | | |

<210> 2
 <211> 187
 <212> PRT
 <213> Homo sapiens

<400> 2

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Pro | Val | Asp | Leu | Ser | Lys | Trp | Ser | Gly | Pro | Leu | Ser | Leu | Gln | Glu |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Val | Asp | Glu | Gln | Pro | Gln | His | Pro | Leu | His | Val | Thr | Tyr | Ala | Gly | Ala |
| | | 20 | | | | | | 25 | | | | | 30 | | |
| Ala | Val | Asp | Glu | Leu | Gly | Lys | Val | Leu | Thr | Pro | Thr | Gln | Val | Lys | Asn |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Arg | Pro | Thr | Ser | Ile | Ser | Trp | Asp | Gly | Leu | Asp | Ser | Gly | Lys | Leu | Tyr |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Thr | Leu | Val | Leu | Thr | Asp | Pro | Asp | Ala | Pro | Ser | Arg | Lys | Asp | Pro | Lys |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| Tyr | Arg | Glu | Trp | His | His | Phe | Leu | Val | Val | Asn | Met | Lys | Gly | Asn | Asp |
| | | | | 85 | | | | | 90 | | | | | 95 | |
| Ile | Ser | Ser | Gly | Thr | Val | Leu | Ser | Asp | Tyr | Val | Gly | Ser | Gly | Pro | Pro |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Lys | Gly | Thr | Gly | Leu | His | Arg | Tyr | Val | Trp | Leu | Val | Tyr | Glu | Gln | Asp |
| | | 115 | | | | | 120 | | | | | 125 | | | |
| Arg | Pro | Leu | Lys | Cys | Asp | Glu | Pro | Ile | Leu | Ser | Asn | Arg | Ser | Gly | Lys |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| His | Arg | Gly | Lys | Phe | Lys | Val | Ala | Ser | Phe | Arg | Lys | Lys | Tyr | Glu | Leu |

145 150 155 160
 Arg Ala Pro Val Ala Gly Thr Cys Tyr Gln Ala Glu Trp Lys Lys Tyr
 165 170 175
 Val Pro Lys Leu Tyr Glu Gln Leu Ser Gly Lys
 180 185

<210> 3
 <211> 187
 <212> PRT
 <213> Mus musculus

<220>
 <221> UNSURE
 <222> (150)..(150)
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 1 5 10 15
 Val Asp Glu Pro Pro Gln His Ala Leu Arg Val Asp Tyr Ala Gly Val
 20 25 30
 Thr Val Asp Glu Leu Gly Lys Val Leu Thr Pro Thr Gln Val Met Asn
 35 40 45
 Arg Pro Ser Ser Ile Ser Trp Asp Gly Leu Asp Pro Gly Lys Leu Tyr
 50 55 60
 Thr Leu Val Leu Thr Asp Pro Asp Ala Pro Ser Arg Lys Asp Pro Lys
 65 70 75 80
 Phe Arg Glu Trp His His Phe Leu Val Val Asn Met Lys Gly Asn Asp
 85 90 95
 Ile Ser Ser Gly Thr Val Leu Ser Asp Tyr Val Gly Ser Gly Pro Pro
 100 105 110
 Ser Gly Thr Ser Ile His Arg Tyr Val Trp Leu Val Tyr Glu Gln Glu
 115 120 125
 Gln Pro Leu Ser Cys Asp Glu Pro Ile Leu Ser Asn Lys Ser Gly Asp
 130 135 140
 Asn Arg Gly Lys Phe Xaa Val Glu Thr Phe Arg Lys Lys Tyr Asn Leu
 145 150 155 160
 Gly Ala Pro Val Ala Gly Thr Cys Tyr Gln Ala Glu Trp Asp Asp Tyr

| | | | | | | | | | | | | | | | |
|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | 165 | | 170 | | 175 | | | | | | | | | | |
| Val | Pro | Lys | Leu | Tyr | Glu | Gln | Leu | Ser | Gly | Lys | | | | | |
| | 180 | | | | | | 185 | | | | | | | | |
| <p><210> 4 <211> 187 <212> PRT <213> Drosophila</p> <p><400> 4</p> | | | | | | | | | | | | | | | |
| Met | Ser | Asp | Ser | Thr | Val | Cys | Phe | Ser | Lys | His | Lys | Ile | Val | Pro | Asp |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Ile | Leu | Lys | Thr | Cys | Pro | Ala | Thr | Leu | Leu | Thr | Val | Thr | Tyr | Gly | Gly |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Gly | Gln | Val | Val | Asp | Val | Gly | Gly | Glu | Leu | Thr | Pro | Thr | Gln | Val | Gln |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Ser | Gln | Pro | Lys | Val | Lys | Trp | Asp | Ala | Asp | Pro | Asn | Ala | Phe | Tyr | Thr |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Leu | Leu | Leu | Thr | Asp | Pro | Asp | Ala | Pro | Ser | Arg | Lys | Glu | Pro | Lys | Phe |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| Arg | Glu | Trp | His | His | Trp | Leu | Val | Val | Asn | Ile | Pro | Gly | Asn | Gln | Val |
| | | | | 85 | | | | | 90 | | | | | 95 | |
| Glu | Asn | Gly | Val | Val | Leu | Thr | Glu | Tyr | Val | Gly | Ala | Gly | Pro | Pro | Gln |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Gly | Thr | Gly | Leu | His | Arg | Tyr | Val | Phe | Ile | Val | Phe | Lys | Gln | Pro | Gln |
| | | 115 | | | | | 120 | | | | | 125 | | | |
| Lys | Leu | Thr | Cys | Asn | Glu | Pro | Lys | Ile | Pro | Lys | Thr | Ser | Gly | Asp | Lys |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| Arg | Ala | Asn | Phe | Ser | Thr | Ser | Lys | Phe | Met | Ser | Lys | Tyr | Lys | Leu | Gly |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| Asp | Pro | Ile | Ala | Gly | Asn | Phe | Phe | Gln | Ala | Gln | Trp | Asp | Asp | Tyr | Val |
| | | | | 165 | | | | 170 | | | | | | 175 | |
| Pro | Lys | Leu | Tyr | Lys | Gln | Leu | Ser | Gly | Lys | Lys | | | | | |
| | | | 180 | | | | | 185 | | | | | | | |

<210> 5
 <211> 220
 <212> PRT
 <213> C. elegans

<400> 5

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|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|
| Met | Val | Val | Leu | Val | Thr | Arg | Ser | Leu | Leu | Pro | Ala | Leu | Phe | Phe | Ala | | | |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | | | | |
| Ser | Arg | Ala | Pro | Phe | Ala | Ala | Ala | Thr | Thr | Ser | Ala | Arg | Phe | Gln | Arg | | | |
| | | | 20 | | | | | 25 | | | | | 30 | | | | | |
| Gly | Leu | Ala | Thr | Met | Ala | Ala | Glu | Ala | Phe | Thr | Lys | His | Glu | Val | Ile | | | |
| | | 35 | | | | | 40 | | | | | 45 | | | | | | |
| Pro | Asp | Val | Leu | Ala | Ser | Asn | Pro | Pro | Ser | Lys | Val | Val | Ser | Val | Lys | | | |
| | 50 | | | | | 55 | | | | | 60 | | | | | | | |
| Phe | Asn | Ser | Gly | Val | Glu | Ala | Asn | Leu | Gly | Asn | Val | Leu | Thr | Pro | Thr | | | |
| 65 | | | | | 70 | | | | 75 | | | | | 80 | | | | |
| Gln | Val | Lys | Asp | Thr | Pro | Glu | Val | Lys | Trp | Asp | Ala | Glu | Pro | Gly | Ala | | | |
| | | | | 85 | | | | | 90 | | | | | 95 | | | | |
| Leu | Tyr | Thr | Leu | Thr | Lys | Thr | Asp | Pro | Asp | Ala | Pro | Ser | Arg | Lys | Glu | | | |
| | | | 100 | | | | | 105 | | | | | 110 | | | | | |
| Pro | Thr | Tyr | Arg | Glu | Trp | His | His | Trp | Leu | Val | Val | Asn | Ile | Pro | Gly | | | |
| | | 115 | | | | | 120 | | | | | 125 | | | | | | |
| Asn | Asp | Ile | Ala | Lys | Gly | Asp | Thr | Leu | Ser | Glu | Tyr | Ile | Gly | Ala | Gly | | | |
| | 130 | | | | | 135 | | | | | 140 | | | | | | | |
| Pro | Pro | Lys | Thr | Gly | Leu | His | Arg | Tyr | Val | Tyr | Leu | Ile | Tyr | Lys | Gln | | | |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 | | | |
| Ser | Gly | Arg | Ile | Glu | Asp | Ala | Glu | His | Gly | Arg | Leu | Thr | Asn | Thr | Ser | | | |
| | | | | 165 | | | | | 170 | | | | | 175 | | | | |
| Gly | Asp | Lys | Arg | Gly | Gly | Trp | Lys | Ala | Ala | Asp | Phe | Val | Ala | Lys | His | | | |
| | | | 180 | | | | | 185 | | | | | 190 | | | | | |
| Lys | Leu | Gly | Ala | Pro | Val | Phe | Gly | Asn | Leu | Phe | Gln | Ala | Glu | Tyr | Asp | | | |
| | | 195 | | | | | 200 | | | | | 205 | | | | | | |
| Asp | Tyr | Val | Pro | Ile | Leu | Asn | Lys | Gln | Leu | Gly | Ala | | | | | | | |
| | 210 | | | | | 215 | | | | | 220 | | | | | | | |

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<211> 181

<212> PRT

<213> Antirrhinum-CEN

<400> 6

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Gly Asp Val Val Asp His Phe Thr Ser Thr Val Lys Met Ser Val Ile
20 25 30

Tyr Asn Ser Asn Asn Ser Ile Lys His Val Tyr Asn Gly His Glu Leu
35 40 45

Phe Pro Ser Ala Val Thr Ser Thr Pro Arg Val Glu Val His Gly Gly
50 55 60

Asp Met Arg Ser Phe Phe Thr Leu Ile Met Thr Asp Pro Asp Val Pro
65 70 75 80

Gly Pro Ser Asp Pro Tyr Leu Arg Glu His Leu His Trp Ile Val Thr
85 90 95

Asp Ile Pro Gly Thr Thr Asp Ser Ser Phe Gly Lys Glu Val Val Ser
100 105 110

Tyr Glu Met Pro Arg Pro Asn Ile Gly Ile His Arg Phe Val Phe Leu
115 120 125

Leu Phe Lys Gln Lys Lys Arg Gly Gln Ala Met Leu Ser Pro Pro Val
130 135 140

Val Cys Arg Asp Gly Phe Asn Thr Arg Lys Phe Thr Gln Glu Asn Glu
145 150 155 160

Leu Gly Leu Pro Val Ala Ala Val Phe Phe Asn Cys Gln Arg Glu Thr
165 170 175

Ala Ala Arg Arg Arg
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<210> 7

<211> 176

<212> PRT

<213> Aradopsis-TFL1

<400> 7

Met Glu Asn Met Gly Thr Arg Val Ile Glu Pro Leu Ile Met Gly Arg
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Val Val Gly Asp Val Leu Asp Phe Phe Thr Pro Thr Thr Lys Met Asn
20 25 30

Val Ser Tyr Asn Lys Lys Gln Val Asn Gly His Glu Leu Phe Pro Ser
35 40 45

Ser Val Ser Ser Lys Pro Arg Val Glu Ile His Gly Gly Asp Leu Arg
 50 55 60
 Ser Phe Phe Thr Leu Val Met Ile Asp Pro Asp Val Pro Gly Pro Ser
 65 70 75 80
 Asp Pro Phe Leu Lys Glu His Leu His Trp Ile Val Thr Asn Ile Pro
 85 90 95
 Gly Thr Thr Asp Ala Thr Phe Gly Lys Glu Val Val Ser Tyr Glu Leu
 100 105 110
 Pro Arg Pro Ser Ile Gly Ile His Arg Phe Val Phe Val Leu Phe Arg
 115 120 125
 Gln Lys Gln Arg Arg Val Ile Phe Pro Asn Ile Pro Ser Arg Asp His
 130 135 140
 Phe Asn Thr Arg Lys Phe Ala Val Glu Tyr Asp Leu Gly Leu Pro Val
 145 150 155 160
 Ala Ala Val Phe Phe Asn Ala Gln Arg Glu Thr Ala Ala Arg Lys Arg
 165 170 175

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 <211> 219
 <212> PRT
 <213> Yeast

<400> 8

Met Asn Gln Ala Ile Asp Phe Ala Gln Ala Ser Ile Asp Ser Tyr Lys
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 Lys His Gly Ile Leu Glu Asp Val Ile His Asp Thr Ser Phe Gln Pro
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 Ser Gly Ile Leu Ala Val Glu Tyr Ser Ser Ser Ala Pro Val Ala Met
 35 40 45
 Gly Asn Thr Leu Pro Thr Glu Lys Ala Arg Ser Lys Pro Gln Phe Gln
 50 55 60
 Phe Thr Phe Asn Lys Gln Met Gln Lys Ser Val Pro Gln Ala Asn Ala
 65 70 75 80
 Tyr Val Pro Gln Asp Asp Asp Leu Phe Thr Leu Val Met Thr Asp Pro
 85 90 95
 Asp Ala Pro Ser Lys Thr Asp His Lys Trp Ser Glu Phe Cys His Leu
 100 105 110

Val Glu Cys Asp Leu Lys Leu Leu Asn Glu Ala Thr His Glu Thr Ser
 115 120 125
 Gly Ala Thr Glu Phe Phe Ala Ser Glu Phe Asn Thr Lys Gly Ser Asn
 130 135 140
 Thr Leu Ile Glu Tyr Met Gly Pro Ala Pro Pro Lys Gly Ser Gly Pro
 145 150 155 160
 His Arg Tyr Val Phe Leu Leu Tyr Lys Gln Pro Lys Gly Val Asp Ser
 165 170 175
 Ser Lys Phe Ser Lys Ile Lys Asp Arg Pro Asn Trp Gly Tyr Gly Thr
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 Pro Ala Thr Gly Val Gly Lys Trp Ala Lys Glu Asn Asn Leu Gln Leu
 195 200 205
 Val Ala Ser Asn Phe Phe Tyr Ala Glu Thr Lys
 210 215

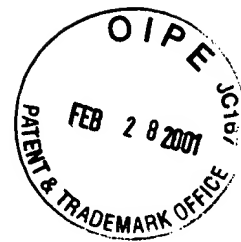
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 catcatttcc tgggtggtcaa catgaagggc aatgacatca gcagtggcac agtcctctcc 12
 0
 gattatgtgg gctcggggcc tccaagggc acaggcctgc accgctatgt ctggctggtt 18
 0
 tacgagcag 18
 9

<210> 10
 <211> 7
 <212> DNA
 <213> Artificial/Unknown

<220>
 <221> Unsure
 <222> (4)..(4)
 <223> n = C or G

<220>



<221> misc_feature
<222> ()..()
<223> Consensus AP-1 binding site

B2
conclude
<400> 10
tgantca

7

<210> 11
<211> 11
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<213> Artificial/Unknown

<220>
<221> misc_feature
<222> ()..()
<223> NF-kB binding element consensus sequence

<400> 11
ggggactttc c
1

1